

# **EXHIBIT 253**

## Actavis Totowa LLC

## Annual Product Review

## Digoxin Tablets, USP 0.25 mg (146)

Reporting Period: January 1, 2006 – December 31, 2006

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		D. Bitler, Quality Assurance Director	
Reviewed By: <i>Scott Talbot</i>	Date: <i>03/31/07</i>	Reviewed By: <i>[Signature]</i>	Date: <i>4/4/07</i>
S. Talbot, Quality Site Head		J. Shah, Regulatory & Medical Affairs Vice President	
Reviewed By: <i>Rick Dowling</i>	Date: <i>3/9/07</i>	Reviewed By: <i>Ashley G. Nigalaye</i>	Date: <i>4/3/07</i>
R. Dowling, Manufacturing Operations Director		A. Nigalaye, Scientific Affairs Sr. Vice President	

## Production Summary

Total Batches produced during this reporting period: 44

Batch No.	MPR No.	MPR Rev.	Batch Size
60115A	14602	09	4,200,000
60116A	14602	09	4,200,000
60117A	14602	09	4,200,000
60118A	14602	09	4,200,000
60119A	14602	09	4,200,000
60158A	14602	09	4,200,000
60159A	14602	09	4,200,000
60160A	14602	09	4,200,000
60161A	14602	09	4,200,000
60162A	14602	09	4,200,000
60319A	14602	09	4,200,000
60320A	14602	09	4,200,000
60321A	14602	09	4,200,000
60322A	14602	09	4,200,000
60323A	14602	09	4,200,000
60497A	14602	09	4,200,000
60498A	14602	09	4,200,000
60499A	14602	09	4,200,000
60511A	14602	09	4,200,000
60512A	14602	09	4,200,000
60513A	14602	09	4,200,000
60514A	14602	09	4,200,000
60515A	14602	09	4,200,000

EXHIBIT

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PENGAD 800-631-6889

PLAINTIFFS' EXHIBITS 000610

ACTAV 000006437

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60677A	14602	10	4,200,000
60678A	14602	10	4,200,000
60679A	14602	10	4,200,000
60680A	14602	10	4,200,000
60681A	14602	10	4,200,000
60863A	14602	10	4,200,000
60864A	14602	10	4,200,000
60865A	14602	10	4,200,000
61053A	14602	10	4,200,000
61054A	14602	10	4,200,000
61055A	14602	10	4,200,000
61056A	14602	10	4,200,000
61057A	14602	10	4,200,000
61097A	14602	10	4,200,000
61098A	14602	10	4,200,000
61099A	14602	10	4,200,000
61100A	14602	10	4,200,000
61101A	14602	10	4,200,000
61102A	14602	10	4,200,000
61103A	14602	10	4,200,000
61104A	14602	10	4,200,000

**Summary of Analytical Data**

See attached data table for details.

All results were within limits. No shifts or trends were observed.

All current specifications continue to be valid.

All yields were within the limits.

**Review of Planned Deviations**

No planned deviations were conducted for this product during the reporting period.

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#### **Review of Investigations**

No investigations were conducted for this product during the reporting period.

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#### **Review of Stability Data**

The following stability samples were evaluated during this reporting period:

- The 36 month interval for batch number 3490A1, fill count 100 (This is the last interval for this batch)
- The 36 month interval for batch number 3490A, fill count 5000 (This is the last interval for this batch)
- The 18 month and 24 month intervals for batch number 4692A, fill count 100
- The 12 month and 18 month intervals for batch number 4696A1, fill count 5000
- The 9 month, 12 month and 18 month intervals for batch number 5291A1, fill count 100
- The 9 month, 12 month and 18 month intervals for batch number 5291A, fill count 5000
- The initial, 13 week and 6 month intervals for batch number 60319A1, fill count 100
- The initial, 13 week and 6 month intervals for batch number 60319AQ, fill count 5000

All results were within limits and the test results were comparable between the 8 batches.

No significant trends were observed.

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#### **Review of Customer Complaints / Adverse Event Reports**

Two customer product complaints were received for this product during the reporting period:

Complaint number C06-095, batch number unknown was for tablets do not break at score. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-166, batch number 5654A1 was for tablet discoloration. No samples were returned. Upon evaluation, the batch documentation was reviewed and indicated no deviations during manufacturing and all in-process checks met the required guidelines. The retain samples were inspected and a few tablets exhibited one or two very small brown spots. The discolored tablets were submitted to the Quality Control

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Laboratory for Impurities testing. The results did not show anything unusual; and no unknown impurities were identified. The brown spotting could be due to the lactose material. No further action is required.

The following 17 adverse events were reported for this product during the reporting period:

Complaint number C06-009, batch number unknown was for an atrial fibrillation. Samples were returned for evaluation. Upon evaluation, the pharmacy was contacted to find out the lot number, but they do not keep the records. Since the lot number is unknown, the in-house retain samples and documentation could not be evaluated. The patient's samples were received and were submitted to the Quality Control Lab for Uniformity of Dosage. The results were within specification limits.

Complaint number C06-030, batch number 5292A1 was for irregular heart beat. No samples were returned for evaluation. Upon evaluation, the retain samples and batch documentation were reviewed. The review of the batch record indicated no problems during manufacturing and the batch was processed as per MPR instructions and no deviations were noted. The evaluation of the retain samples showed no tablet degradation or order. Retain samples were submitted to the Quality Control Laboratory for Assay testing and the results were within specification limits.

Complaint number C06-046, batch number unknown was for an elevated digoxin level, bradycardia. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-056, batch number unknown was for orthostatic hypotension. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-057, batch number unknown was for increased serum levels of ammonia and alkaline phosphatase. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-058, batch number unknown was for a potency question. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-062, batch number unknown was for heavy chest pain and tiredness. No samples were returned. Upon evaluation, a thorough investigation could not be performed due the lot number being unknown. No further action is required.

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Complaint number C06-066, batch number unknown was for blurry vision. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-094, batch number unknown was for a CHF. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-115, batch number unknown was for orthostatic hypotension. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-117, batch number unknown was for thrombocytopenia. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-118, batch number unknown was for bradycardia and hematochezia. No samples were returned. Upon evaluation, a thorough investigation could not be performed due the lot number being unknown. No further action is required.

Complaint number C06-124, batch number unknown was for blood pressure not decreasing like it should. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-127, batch number unknown was for patient tolerance. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-135, batch number unknown was for an acute heart failure. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-141, batch number unknown was for trembling hands/feet & unstable walking. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

Complaint number C06-161, batch number unknown was for patient becoming confused. No samples were returned. Upon evaluation, a thorough investigation could not be performed due to the lot number being unknown. No further action is required.

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#### **Review of Formula / Process Changes**

No formula or process changes were made for this product during the reporting period.

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#### **Review of MPR / Specifications Changes**

MPR 14602 rev. 09 was revised to 14602 rev. 10 for this product during the reporting period. The changes were as follows:

- Changed company name to "Actavis Totowa LLC" throughout the document.
- Removed "...and alcohol content of Oxycodone Hydrochloride, USP" and replaced it with "...moisture content of Digoxin Micronized, USP" in the Master Formula Sheet section.
- Deleted an additional row from the table in step 29 in the Blending section.

No specification changes were made for this product during the reporting period.

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#### **Review of Process Validation**

No process validation was conducted for this product during the reporting period.

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#### **Trend Evaluations / Conclusions**

Line graphs are attached for Final Blend Assay, Compression Weight, Compression Hardness, Compression Thickness, Content Uniformity, Dissolution, Assay and Percent Yield.

All data was reviewed and no significant trends were observed. However, for batch number 60319A, the Final Blend Assay Standard Deviation value was 4.5% which was higher than the other batches reviewed. All Final Blend Assay data were reviewed and were within specification limits. For batch number 61057A and forward, the QC Laboratory used the Acceptance Value criteria instead of the Content Uniformity RSD values due to a change in the USP. For batch number 60512A, the Dissolution Standard Deviation value was slightly higher compared to the other batches reviewed. All Dissolution data were reviewed and were within specification limits. For batch number 60681A, the Assay value was slightly higher compared to the other batches reviewed. All Assay data were reviewed and were within specification limits.

Revisions are not required for Formula/Process or MPR/Specifications.

No revalidation of the process is required.